

CLAIMS

What is claimed is:

1. A compound comprising arginine deiminase covalently bonded via a linking group to polyethylene glycol,
wherein the arginine deiminase is derived from a microorganism of the genus selected from the group consisting of: *Streptococcus*, *Borrelia*, *Qiardia*, *Clostridium*, *Enterococcus*, *Lactobacillus*, and *Bacillus*;
wherein the polyethylene glycol has a total weight average molecular weight of from about 1,000 to about 40,000, and
wherein the linking group is selected from the group consisting of a succinimide group, an amide group, an imide group, a carbamate group, an ester group, an epoxy group, a carboxyl group, a hydroxyl group, a carbohydrate, a tyrosine group, a cysteine group, a histidine group and combinations thereof.
2. The compound of claim 1, wherein said linking group is a succinimide group.
3. The compound of claim 2, wherein said succinimide group is succinimidyl succinate, succinimidyl propionate, succinimidyl carboxymethylate, succinimidyl succinamide, N-hydroxy succinimide or combinations thereof.
4. The compound of claim 3, wherein said succinimide group is succinimidyl succinate, succinimidyl propionate or combinations thereof.
5. The compound of claim 1, wherein said microorganism is selected from the group consisting of *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Borrelia burgdorferi*, *Borrelia afzelii*, *Qiardia intestinalis*, *Clostridium perfringens*, *Enterococcus faecalis*, *Lactobacillus sake*, *Bacillus licheniformis* and combinations thereof.
6. The compound of claim 1, wherein said arginine deiminase is derived from a microorganism of the genus *Streptococcus*.
7. The compound of claim 6, wherein said microorganism is selected

from the group consisting of *Streptococcus pyogenes*, *Streptococcus pneumoniae* and combinations thereof.

8. The compound of claim 1, wherein said arginine deiminase is derived from a microorganism of the genus *Borrelia*.

9. The compound of claim 8, wherein said microorganism is selected from the group consisting of *Borrelia burgdorferi*, *Borrelia afzelii*, and combinations thereof.

10. The compound of claim 1, wherein said arginine deiminase is derived from a microorganism of the genus *Qiardia*.

11. The compound of claim 10, wherein said microorganism is *Qiardia intestinalis*.

12. The compound of claim 1, wherein said arginine deiminase is derived from a microorganism of the genus *Clostridium*.

13. The compound of claim 12, wherein said microorganism is *Clostridium perfringens*.

14. The compound of claim 1, wherein said arginine deiminase is derived from a microorganism of the genus *Enterococcus*.

15. The compound of claim 14, wherein said microorganism is *Enterococcus faecalis*.

16. The compound of claim 1, wherein said arginine deiminase is derived from a microorganism of the genus *Lactobacillus*.

17. The compound of claim 16, wherein said microorganism is *Lactobacillus sake*.

18. The compound of claim 1, wherein said arginine deiminase is derived from a microorganism of the genus *Bacillus*.

19. The compound of claim 18, wherein said microorganism is *Bacillus licheniformis*.

20. The compound of claim 1, wherein said arginine deiminase is covalently bonded to about 7 to about 15 polyethylene glycol molecules.

21. The compound of claim 20, wherein said arginine deiminase is covalently bonded to about 9 to about 12 polyethylene glycol molecules.

22. The compound of claim 1, wherein said polyethylene glycol has a total weight average molecular weight of from about 10,000 to about 30,000.

23. A method of enhancing the circulating half life of arginine deiminase comprising modifying said arginine deiminase by covalently bonding said arginine deiminase via a linking group to polyethylene glycol,
wherein the arginine deiminase is derived from a microorganism of the genus selected from the group consisting of: *Streptococcus*, *Borrelia*, *Qiardia*, *Clostridium*, *Enterococcus*, *Lactobacillus*, and *Bacillus*;

wherein the polyethylene glycol has a total weight average molecular weight of from about 1,000 to about 40,000, and

wherein the linking group is selected from the group consisting of a succinimide group, an amide group, an imide group, a carbamate group, an ester group, an epoxy group, a carboxyl group, a hydroxyl group, a carbohydrate, a tyrosine group, a cysteine group, a histidine group and combinations thereof.

24. A method of enhancing the tumoricidal activity of arginine deiminase comprising modifying said arginine deiminase by covalently bonding said arginine deiminase via a linking group to polyethylene glycol,

wherein the arginine deiminase is derived from a microorganism of the genus selected from the group consisting of: *Streptococcus*, *Borrelia*, *Qiardia*, *Clostridium*, *Enterococcus*, *Lactobacillus*, and *Bacillus*;

wherein the polyethylene glycol has a total weight average molecular weight of from about 1,000 to about 40,000, and

wherein the linking group is selected from the group consisting of a succinimide group, an amide group, an imide group, a carbamate group, an ester group, an epoxy group, a carboxyl group, a hydroxyl group, a carbohydrate, a tyrosine group, a cysteine group, a histidine group and combinations thereof.

25. A method of treating a tumor in a patient comprising administering to said patient the compound of Claim 1.

26. The method of claim 25, wherein said tumor is a melanoma.

27. The method of claim 26, wherein said polyethylene glycol has a total weight average molecular weight of about 20,000

28. The method of claim 26, wherein said linking group is a succinimide group.

29. The method of claim 28, wherein said succinimide group is succinimidyl succinate, succinimidyl propionate, succinimidyl carboxymethylate, succinimidyl succinamide, N-hydroxy succinimide or combinations thereof.

30. The method of claim 25, wherein said tumor is a hepatoma.

31. The method of claim 30, wherein said polyethylene glycol has a total weight average molecular weight of about 5,000

32. The method of claim 30, wherein said linking group is a succinimide group.

33. The method of claim 32, wherein said succinimide group is succinimidyl succinate, succinimidyl propionate, succinimidyl carboxymethylate, succinimidyl succinamide, N-hydroxy succinimide or combinations thereof.

34. The method of claim 25, wherein said tumor is a sarcoma.

35. A method of treating and inhibiting metastases in a patient comprising administering to said patient the compound of claim 1.